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(54) Title: HOMOGENOUS SOLID MATRIX CONTAINING VEGETABLE PROTEINS

(57) Abstract: The invention provides a homogenous solid matrix composition, enabling an improved dispersion of and bitter taste masking of hydrophobic, bioactive ingestibles, of at least low water solubility comprising: (a) at least 10 % w/w vegetable proteins; (b) lecithin; and (c) at least one ingestible bioactive compound of at least low water solubility.

HOMOGENOUS SOLID MATRIX CONTAINING VEGETABLE PROTEINS

The present invention relates to a homogeneous solid matrix composition containing vegetable proteins, lecithin and an ingestible bioactive compound of at least low water solubility. The term, at least low-water solubility, as used herein, is intended to denote a compound having low or poor water solubility as well as compounds which are water insoluble due to the presence of at least a hydrophobic moiety in the compound or, the hydrophobicity of the compound as a whole.

The bioactive compound is homogeneously embedded in an amorphous, non-crystalline form in the matrix for achieving the advantages of enhanced dissolution and biological availability of said ingestible, bioactive compound to be administered to mammals, as well as taste masking of bitter ingestable substances.

This invention has been developed to provide an answer for an unmet therapeutic or nutraceutic need of low biological availability of: drugs, phytomedicines, phytonutrients, vitamins and nutraceutical or food supplements, especially herbal extracts comprising variable levels of assembly of hydrophobic constituents, which do not mix or disperse well enough in the gastrointestinal physiological fluids. These have a low dissolution, low oral bioavailability and large inter-individual availability variation, which is an obstacle for their full exploitation.

Since most bitter tasting compounds are poorly water soluble or at least have a hydrophobic moiety, this invention has been developed to give an answer for an unmet therapeutic or nutraceutic need of rejected and undesired bitter tasting drugs or nutrients.

Description of the prior art

A variety of solid matrix compositions and production techniques have been used for years by the pharmaceutical and food industry in order to:

a) convert liquids to free-flowing powder,

b) improve the dissolution rates and bioavailabilities of drugs, specifically of insoluble or of low solubility,

c) protect the compounds from decomposition, and

d) mask unfavorable odor or taste.

Such methods and matrices include particular solids in the form of: microencapsules, microspheres, granules, pellets, nano-particles, etc.

Microparticles are spherical polymeric particles ranging in size from greater than one micron, up to 2000 microns. Microparticles include microcapsules in which the biological agent is uniformly confined within a cavity, and microspheres in which the agent is dispersed throughout the microparticle. The agent may be dispersed in the microparticle matrix as discrete crystals or in an amorphous homogeneous form. Many processes can be used for the preparation of microparticles including solvent evaporation, organic phase separation, interfacial polymerization, emulsion polymerization, and spray drying.

Numerous polymers have been used as matrices for microparticles including polysaccharides, polyesters, and nonbiodegradable synthetic polymers. Polyesters, especially, poly(D,L-lactide-co-glycolide) are desirable for microencapsulation of peptides because aside from being biodegradable or bioerodible, they are also readily available, easily processed and non-toxic.

Matrices and microparticles are also prepared from bio-compatible materials such as starch, cross linked starch, starch derivatives and modified starches including: amylodextrin, gelatin, albumin, collagen, dextrin and dextrin derivatives, polyvinyl alcohol, polylactide-co-glycolide, hyaluronic acid and derivatives thereof, such as benzyl and ethyl esters, gellan gum and derivatives, cellulosic polymers, specifically lower alkyl ethers of cellulose in addition to protein polymers such as albumin, sephadex, or DEAE-sephadex.

Other known materials used in manufacturing microparticles include alginates, xanthan gum, and gellan gum. All three substances are effective as enteric coatings. Alginates are known to produce uniform films and are applied in industries as diverse as paper coatings, textile printing, and foods. The alginate film is particularly effectual as an enteric coating because it normally is applied as the soluble sodium form, which then is converted to the insoluble alginic acid form by gastric fluids. Improvements have been made by combining sodium alginate with sodium calcium alginate in tablets containing high drug loading.

US patent 5,972,387 discloses a "modified vegetable protein" to produce microspheres for oral delivery of pharmaceutical agents. The "vegetable protein" is

modified with benzene sulfonyl chloride and benzoyl chloride. The present invention makes it possible to produce microspheres with non-modified vegetable proteins.

US patents 5,558,880 and 5,684,093 "relate to methods for preparing products by removal of a solid frozen solvent from a frozen matrix mixture". A fast dissolving porous solid matrix is formed, containing small amounts of gelatin, pectin and/or soy fiber protein as an anti cracking and anti meltback.

US patent 5,725,899 "relates to a novel composition of lipoprotein material having emulsification and gel-forming properties and more particularly to such a composition prepared from edible soy flour". This patent discloses the use of a defatted oil-seed protein material, in contrast to the present invention which makes use of concentrated or isolated vegetable proteins. This patent also aims to produce emulsifying and gelling agents and not a solid lipid matrix.

Synthetic proteins are used for microencapsulation. For example, US patent 5,840,340, uses small proteins, 25 to 2400 daltons or 2 to 20 amino acids, to form "protenoid carriers" with solubility within selected pH ranges, for oral delivery of pharmaceutical agents. US patent 5,904,936 applies synthetic polyamino acids of specific type in the range of 4,000 daltons. The present invention utilizes all natural, non-synthetic, vegetable proteins of 25,000 daltons and higher.

Co-precipitation is a common method for obtaining homogeneous, non-crystalline dispersions of an agent in a specific matter. Preparing such solid particles including microparticles, microspheres, microcapsules, nanoparticles, pellets or granules, and the incorporation of ingestible bioactive compounds, involves the use of synthetic polymers and organic solvents. For example, US patent 6,004,973 uses organic solvent, ethanol/acetone, to produce nanparticles made of synthetic polymers containing Rafamycin in a non-crystalline amorphous dispersion. US patent 5,776,495 utilizes a range of organic solvents, such as methylene chloride, alkanols, chlorinated and oxygenated solvents, in order to produce solid co-precipitates. US patent 5,491,154 employs acetone to co-precipitate dihydropyridines with PVP. US patent 4,880,623 uses acetone; methylene chloride to co-precipitate Nifedipine with polyethylene glygol and hydroxypropylmethylcellulose; methylcellulose; hydroxypropylcellulose;

carboxyvinyl polymers; and xanthan gum. US patent 4,758,427 teaches solid molecular dispersion of 2-aryl-pyrazolo quinolines with PVP, co-precipitated by the use of methanol. US patent 4,610,875 makes enhanced dissolution of dipyridamole in amorphous form in PVP, using organic solvents and an agent inhibiting the formation of crystals. The present invention does not make use of organic solvents or synthetic polymers, although it does enable co-precipitation of ingestible bioactive compounds in a homogeneous solid matrix made of vegetable ingredients.

US patent 4,404,228 relates to a lipid and protein containing material in particulate form. Such materials are widely used in the human and animal foodstuff industries, including calf milk substitutes and coffee whiteners.

Bitter tasting agents are generally administered orally in gelatin capsules or coated tablets, however, other methods for taste masking of bitter compounds are available, including mixing the substance with taste modifying agents, granulating or microencapsulation. US patent 5,904,937 discloses use of microcrystaline cellulose for wet granulation of bitter drugs. US patent 5,728,403 discloses coating technology for taste masking orally administered bitter drugs. US patent 5,382,535 discloses "chewable drug-delivery compositions" for oral delivery of unpalatable drugs. The drug is intimately dispersed or dissolved in a pharmaceutically acceptable lipid that is solid at room temperature. US patent 5,785,984 discloses a "protein-lipid complex which modifies the taste of a food, pharmaceutical or cosmetic". The "protein-lipid complex" agent, acts with the sensory taste to block out and reduce the sensation of bitterness. This patent also teaches the use of organic solvents for incorporating hydrophobic ingestibles. This patent does not teach the use of a homogeneous solid matrix where ingestible bioactive compounds are embedded in a non-crystaline amorphous manner. US patent 5,972,373 discloses compositions for taste masking and bioavailability with synthetic stomach soluble polymers and monoglyceride in a beta-crystal form. The disclosed polymers are: polyvinylacetal diethylaminoacetate, aminoalkylmethacrylate copolymer E or a mixture thereof.

Summary of the Invention

According to the present invention there is provided a novel composition of a homogeneous solid matrix of various shapes, that absorb water, swell and form suspended gel or hydrated particles, for administration of ingestible, bioactive compounds of at least low water solubility as hereinbefore defined, and which compositions improve gastro-intestinal dissolution and consequent oral availability or bio-compatibility, in addition to taste masking of bitter drugs, nutrients, food additives, vitamins, minerals or phytomedicines.

Thus, according to the present invention, there is now provided a homogeneous solid matrix composition, enabling an improved dispersion of and bitter taste masking of hydrophobic, bioactive ingestibles, of at least low water solubility comprising:

(a) at least 10% w/w functional vegetable proteins;

(b) lecithin; and

(c) at least one ingestible bioactive compound of at least low water solubility.

In preferred embodiments of the present invention said composition comprises at least 20% w/w vegetable proteins and in especially preferred embodiments of the present invention said composition comprises at least 40% w/w vegetable proteins.

The composition of the present invention includes:

(a) the required amount of ingestable bioactive drugs, nutrients or phytomedicines to achieve the desired physiological benefit;

(b) functional vegetable proteins of the type and in an amount sufficient to produce and support solid dry matrix; and

(c) lecithin, in sufficient amounts, to enable solvent free water solubilization of various hydrophobic bioactives, having limited solubility in water.

According to a preferred embodiment of the present invention, the hydrophobic bioactive and ingestible ingredients are solubilized and/or co-melted with required amounts of lecithin-water mixture, until homogeneity is achieved. Homogeneity is defined as absence of crystalline form of the ingestible bioactive

compound. The homogeneous wet mixture is further mixed with vegetable proteins to homogeneity, sufficient water is added to produce a desired consistency appropriate for screen granulation, sieving and shaping. Said mixture is finally molded and dried for the desired shape. The final mixing with vegetable proteins and the drying step may also be accomplished simultaneously in case such as spray drying.

According to a preferred embodiment of the present invention, the solubilization is a solvent free process whereby the hydrophobic, low or poor water soluble compounds, are solubilized within the hydrated lecithin aggregates`s hydrophobic and amphiphilic micro-environments.

In preferred embodiments of the present invention, there is provided a composition comprising lecithin and said ingestible bioactive compound in relative amounts of 1:4 to 4:1, preferably 1:2 to 2:1 and most preferred in relative amounts of 1:1.

In especially preferred embodiments of the present invention, the ratio of vegetable protein to the combined amounts of lecithin and ingestible bioactive compound is between 20:1 to 1:4, preferably 10:1 to 1:2 and most preferably the ratio is between 3:1 and 1:1.

Various vegetable proteins possessing diversity of functionality levels which directly influence the matrix formation, its density and the required amount of protein to obtain the matrix. More functional vegetable proteins are forming denser three dimensions network, enabling formation of the matrix at lower protein concentration or forming much tighter condensed matrix.

The active compounds are released from the homogeneous solid matrix in a non-immediate manner. By selecting proteins with different functionality and at different concentration, the magnitude of delaying the release is controlled. For purposes of masking bitter taste, there is a need for short delay of release, while the granules are passing the oral cavity. A hydrophobic compound will be released from a very tight matrix in a slow release manner. The current invention enable control and design of the release pattern from very short release delay for purpose of taste masking to prolonged delay of as long as couple of hours for effective absorption and lowering number of daily administrations.

Water soluble, hydrophylic, compound will be very fast released from the matrix whereas hydrophobic compounds will be released mostly at the small intestine as the proteins are digested and the matrix decomposes.

Thus, in preferred embodiments of the present invention said matrix provides for the release of said ingestible bioactive compound over a period of one to three hours in the gastro-intestinal tract.

In especially preferred embodiments of the present invention the limiting step for the ingestible bioactive compound release is the gastro-intestinal digestion of said proteins and decomposition of the matrix.

The release rate is also influenced from the amount of lecithin in the matrix. High lecithin concentration enhance the release profile due to better hydration, swelling and decomposing of the matrix.

As defined hereinbefore, the compounds of the present invention, have at least low water solubility and especially preferred are ingestible bioactive compounds having a water solubility of less then 0.5 mg/ml at 25 °C. Also compositions or mixtures, such as plant extracts, comprising such at least low water soluble fractions.

In a further preferred embodiment of the present invention, the drying process may be performed by heat, circulating hot air, microwave, a combination of heat and vacuum, lyophilization or sprat dry.

According to a further preferred embodiment of the present invention, the ingestible bioactive compound or mixture is homogeneously embedded in the final matrix in a way that the original crystals or powder or amorphous solid does not exist, and the dispersability in the matrix is uniform, so that the matrix is a monolithic entity, made up of an even homogeneous distribution of the various ingredients; actives and excipients.

According to a preferred embodiment of the present invention, additives, such as fumed silica may be added before or after drying, in order to advance flowing properties of resulting powder.

According to a preferred embodiment of the present invention, additives such as pharmaceutical or food grade emulsifiers, or gliding agents, may be added

before or after drying in order to advance the free flowing properties of resulting powder.

According to a preferred embodiment of the present invention, the composition may include additives such as colorants, ant-oxidants, preservatives, etc. known in the art for nutraceuticals, food or medicines.

According to a preferred embodiment of the present invention, the composition may include within the primary composition or added to the post drying product taste and flavoring agents known in the art for nutraceuticals, food or medicines, such as fruits flavors or instant fruits powders for reconstitution as beverage.

According to a preferred embodiment of the present invention, the resulting dry solid matrix may be shaped as granules, pellets, microspheres, nanoparticles, in addition to irregular shapes of various sizes and quantities.

The ratio of the amount of hydrophobic bioactive mixture or bitter compound, and the lecithin and vegetable proteins, is adjustable according to the nature of the bioactive compound, and is adequately designed by those skilled in the art.

The compositions are well suited for pharmaceutical use, complementary medicine, nutraceutical and veterinary use, as well as for oral consumption in the shape of bars, nuggets, tablets, capsules, coated tablets or capsules, dissolve-in-the-mouth tablets, effervescent tablets or powder, concentrated powders for in situ, instant, juice or beverage preparations and confectionery, etc.

According to another embodiment of the present invention, there is provided a method of releasing the ingestible bioactive from the homogeneous solid matrix. Hereinafter, the term "subject" is the human or mammal to which the homogeneous matrix of the present invention is administered.

In another aspect of the present invention, there is provided a method for preparing the composition of claim 1, wherein lecithin is swollen in water in a ratio of between about 1:3 to 1:10 more preferable 1:5 to 1:8 and said ingestible bioactive compound is added until complete solubilization, functional vegetable proteins is then added with additional water, if necessary and in quantum sufficient, to produce granulation dough, whereafter, the wet mass is granulated and dried.

In another embodiment, the resulting granules are spread evenly on large pieces of paper in shallow trays and dried in dedicated regulated heat oven, hot circulating oven, or microwave oven or under reduced pressure and temperature or fluid bed drier.

In preferred embodiments of this method said wet mass is further diluted with water and spray dried.

In further preferred embodiments of the method, the wet granulation is extruded through a screen having openings of 0.5 mm to 2.5 mm and spheronized in a spheronizer.

In yet further preferred embodiments, of said method the wet granulation is prepared and formed into spheres, utilizing a high shear granulator to form taste-masked spheres.

Preferably, said method is applied to an ingestible bioactive compound, which is a bitter tasting compound, and homogeneous particles and taste masking are obtained.

Functional vegetable proteins that are suitable for solid matrix forming have the following physico-chemical characteristics:

A) high molecular weight of 50,000 daltons and higher

B) NSI (nitrogen solubility index) of at least 10% and preferably higher then 20%, and

C) non-denaturated or only partially denaturated proteins.

Therefore, said vegetable proteins are non or minimally denturated, having at least 10% NSI with a preferred NSI of 20% and an even more preferred, higher NSI and MW of not less then 50 kD with a range of 100,000 to 300,000 MW, non or minimally hydrolyzed.

Vegetable proteins may be protein concentrates or protein isolates of: soy (soybeans), wheat and wheat germ, barley, sesame, pea, rice, beans, peanuts, potatoes, legume, corn, sunflower, canola or rapeseed.

Said functional vegetable proteins should contain at least 65% Protein (N.times.6.25) mfb and.

The soybean, Glycine max, is a leguminous crop grown in many parts of the world. Soybeans are of great economic importance as a source of edible oil,

high-protein foods, food ingredients, and stockfeed, as well as many industrial products. Native to Eastern Asia, the soybean has been used as the chief source of protein for millions of people in the Orient, for centuries. It was not until the late 19th century, however, that soybeans began to attract serious attention from Western scientists.

The term "soy proteins" typically refers to processed, edible dry soybean products other than soybean meals for animals.

Soy protein products, for human consumption, fall into three major groups:

(a) Soy flours and grits having 52 to 54% Protein (N.times.6.25) on a moisture-free basis (mfb),

(b) soy protein concentrates containing at least 65% Protein (N.times.6.25) mfb, and

(c) soy protein isolates (or soy proteinates) having a minimum of 90% Protein (N.times.6.25) mfb.

The term "% Protein (N.times.6.25)" is often used to express the percentage of protein in soy protein products in order to reflect that only part of the nitrogen in soy proteins is of protein origin. The American Oil Chemists' Society (AOCS) conversion factor for soybean protein is N.times.5.71; however, industry practice is to label protein in soybeans as "Protein (N.times.6.25)."

Soy flours and grits are the least refined forms of soy protein products used for human consumption and may vary in fat content, particle size, and degree of heat treatment. These products also still contain about five (5) to six (6)% of the oligosaccharides and most of the original lipoxygenase, as well as about 4.3% fiber. As a result, they can only be used in small amounts in various products; otherwise intestinal discomfort and poor flavor become the overriding consideration. Soy flours and grits are considered to be "poorly" functional and typically have an NSI less than about 60%.

Soy protein concentrates have much of the indigestible oligosaccharides removed and therefore the raffinose content is less than about 0.5% and the stachyose content is less than about three (3)%. However, depending on the process used, soy protein concentrates have only poor to adequate flavor, and low to adequate functionality, having NSI's in the range of 15-70%. Additionally, the

various processes for producing soy protein concentrates result in a recovery of only about 50% to 95% of the protein. In every instance, the high cost of such processes limit the use of these products in many areas such as aquacultural diets, poultry diets, and so forth. Furthermore, the presence of approximately four (4)% fiber in soy protein concentrates makes them unsuitable for use in certain products such as beverages, milk and infant formulas. The current processes also remove important vitamins, minerals, isoflavones and phytoestrogens along with the low molecular-weight sugars, ash, and minor components.

Soy protein isolates are the most highly refined soy protein products commercially available, as well as the most expensive. As with the soy protein concentrates, soy protein isolates are also low in oligosaccharides, having negligible amounts of raffinose and less than two 2(%) stachyose in the final product. Additionally, the isolates have a satisfactory flavor and are highly functional, having a NSI in the range greater than about 85%. Isolates also improve dispersibility and reduce dusting. Both gelling and non-gelling varieties are available in addition to various viscosity grades. They possess a low fiber content of less than about 0.3%. As discussed above, it is desirable to remove the fiber in certain products because fiber is non-functional and dilutes protein content.

Soy Protein Concentrates: Concentrates produced by the aqueous alcohol and heat treatment/water extraction processes have low nitrogen solubility because of protein denaturation. In contrast, the products made by aqueous acid leaching or by steam injection/jet cooking, and subsequent high shear treatment, have higher solubility if neutralized prior to drying. These concentrates vary in particle size, water and fat absorption properties and flavor. They all have improved flavor characteristics compared to commercially available soy flours. They provide several functional characteristics in forming fat emulsions in food systems such as fat-micelle stabilization, water and fat absorption, viscosity control and textural control. Many of these characteristics are inter-related in a stable food system. Both pH and temperature affect the emulsifying properties of soy concentrates.

Soy concentrates contain polysaccharides, which absorb a significant amount of water. Processing conditions can vary the amount of water that can be

absorbed. In fact, these conditions can be varied to influence how tightly the water is bound by the protein in the finished food product.

Since the acid leach and steam injection/jet cooking processes can result in a product with higher dispersibility, these concentrates are more desirable for functional properties in emulsion-type applications. Nevertheless, all soy protein concentrates, regardless of the process used, do have certain fat and water-retaining characteristics.

Soy Protein Isolates: Isolates have specific functional properties that enable them to modify the physical properties of food products. Soy isolates are characterized by certain functional properties i.e., solubility, gelation, emulsification, dispersibility, viscosity and retort stability.

Solubility ranges from 5 NSI (Nitrogen Solubility Index) to 95 NSI. The emulsion capacity of soy protein isolates can vary from 10 to about 35 milliliters of oil per 100 milligrams of protein. Isolates have water absorption values of up to 400% (3).

Neutralized isolates are usually highly soluble; certain types will gel under appropriate aqueous conditions. They possess both emulsifying and emulsion-stabilizing properties, are excellent binders of fat and water, and are good adhesive agents. They vary mainly in their dispersibility, gelling and viscosity characteristics.

Soy protein isolate aids in forming a gel which acts as a matrix for holding moisture, fat and solids. This results in textural properties resembling those of meat proteins, which is especially important for use in comminuted meats and non-meat items such as tofu. Its ability to form a gel (from fragile to firm) depends on concentration, functionality and the presence or absence of salt. Some isolates are designed not to form a gel even at a 14% solids content.

Gelation is the formation of three dimensional, intermolecular networks through hydrogen, hydrophobic, and disulfide bonds that entrap water solvent and other ingredients. This is another aspect of hydration and of textural and rheological properties of protein; further defined as the formation of three dimensional intermolecular networks through hydrogen, hydrophobic, and disulfide bonds that entrap water and other ingredients. This entrapment contributes to the

texture and chewiness of the food products. The important initial step in heat-induced gelation of globular proteins, is heating of the protein solution above the denaturation temperature to expose the functional groups, so that the intermolecular network can be produced. Additionally, high numbers of intermolecular disulfide bonds increase water holding capacity, and, as a result, increases gel hardness.

Wang and Damodaran (1990) studied the thermal gelation of globular protein of bovine serum albumin (BSA), soy isolate, 7S, 11S, and phaseolin. They reported that gel hardness or strength of globular protein gels is fundamentally related to the size and shape of the polypeptide in the gel network, rather than to their chemical nature such as amino acid composition and distribution. Globular protein with MW<23 kD cannot form a self-supporting gel network in any reasonable concentration.

The homogeneous solid matrix is formed during the drying process, whereby the vegetable proteins form the solid matrix by constituting molecular connections between the proteins in a similar or equal process to denaturation.

Example of commercially available isolated soy proteins are the Supro^{R} types 810, 760 and EX 34K and others from Protein Technologies International, St Louis, MO, USA and Soyarich^{R} from Central Soy Protein, USA. Examples of concentrated soy proteins are Solcon HV, and other brands from ADM and Cargill both of USA.

Lecithin is a mixture of phospholipids from vegetable or animal origin; e.g. these may be obtained from soybean, wheat, corn or eggs. More preferably, the lecithin concentration is equal to the amount of the bioactive compound and is present in an amount of not less then 1 percent and up to 50 percent.

Phospholipids are the main building blocks of all cell membranes - in human beings, animals, plants and micro-organisms. As such they have two important physico-chemical properties which are being put to increasing use in pharmaceutical technology:

1) amphiphilic molecules which contain excellent emulsifying properties; and

2) under certain conditions, especially with respect to concentration and temperature, phospholipids spontaneously form membrane structures (lamella, liposomal, micellar).

Products include vegetable (mainly soybean) and animal phospholipid mixtures (egg) with greatly differing compositions and properties, and also hydrogenated products that are especially useful for their resistance to oxidation. Lecithin may also be obtained from various vegetable origins, for example: oatmeal, wheat germ or peanuts.

Historically, the term lecithin originated from the Greek word 'lekithos', which was used for the phosphorus containing lipids from egg yolk. Later, this term was only used for one defined phospholipid, phosphatidylcholine. This is still the common usage in scientific literature, where lecithin stands for 1,2-diacyl-sn-glycero-3-phosphatidylcholine. On the contrary, the industrial and commercial understanding of the term lecithin is used for the complex mixture of neutral lipids (predominantly triglycerides, a small amount of free fatty acids and sterols), polar lipids (phospho- and glycolipids) and carbohydrates.

The technological and physiological properties of lecithins are primarily determined by the kind and portion of the various polar lipids, especially the phospholipids. It is evident that these compositions may vary considerably, depending on the origin of the soybeans. Climate, soil conditions, harvest time and, last but not least, processing conditions, greatly influence the composition and properties of lecithin too.

The molecular structure of phospholipids is derived from the structure of triglycerides by replacement of one fatty acid by a phosphoric acid ester. Depending upon the molecule (predominantly an aminoalcohol) linked to the phosphate group, the various phospholipids are nominated.

Choline = Phosphatdylcholine (PC)

Ethanolamine = Phosphatdylethanolamine (PE)

Inositol = Phosphatdylinositol (PI)

Hydrogen = Phosphatidic acid (PA)

By virtue of their ampiphilic molecular structure with the hydrophilic phosphoric acid ester and the lipophilic fatty acids, phospholipids in oil and water

systems always concentrate at the interphase. This typical emulsifying property is the reason for their successful use in a variety of foodstuffs, dietetic, cosmetic and pharmaceutical preparations.

Lecithin is described as a generally permitted food additive in Europe under E 322 and in the US in the Code of Federal Regulations (GRAS status) referring to the Food Chemical Codex. Both descriptions differ to a minor extent in their specification details, but not in principle.

Example of commercially available lecithins are, Phospholipons from Natterman, Epikurons from Lucas Meyer, Pure lecithin powder de-oiled from Stern, all from Germany, and others.

Insoluble or low water soluble ingestible bioactive compounds may be any chemical, drug, molecule, substance, extract, herbal, vitamin, synthetic or semisynthetic or biotechnology product, hormone, peptide, protein, or mixture comprising such ingredient, that has a desired and or required bio-activity, and its biological activity is reduced, limited or is practically erratic, due to low or poor water solubility and low dissolution or wetting and insufficient concentration at the absorption or administration or biological target site. Most preferably, the bioactive compound is present in an amount of from about 0.1 percent to 50 percent weight of the final product, more preferably in the range of 1.0 to 30%, and is practically dictated by its bio-active dose relevant for the specific use, purpose, expected results and physico-chemical formulation properties.

Hydrophobic, water insoluble or lipophilic agents and low or poor water solubility compounds, as used herein, refer to ingestable agents, having a water solubility of <1mg/ml and, more preferably, <0.5mg/ml in water, at room temperature (25.degree. C.).

Most phytomedicinal extracts are mixtures or assemblies of many types of molecules, usually comprising a fraction that is water insoluble or has low water solubility. With regard to proper and effective herbal extracts, solvents such as alcohol or propylene glycols or glycerin, and hexane or cyclohexane, are frequently and abundantly employed in phytomedicinal extract production. Another method for herbal extraction of water insoluble precious bioactive compound, is lipid extraction, hot or cold compression and super fluid extraction. All these methods

are employed in order to obtain herbal fraction with poor water solubility. The non-aqueous extracts are important constituents of the majority of herbal bioactive products. Apart from few exceptions, most top marketed herbal extracts contain some hydrophobic active molecules of poor water solubility. Many of the herbal extracts, especially those extracted from lower underground root parts of the herbs, are also typically bitter.

Examples of herbal, poorly water-soluble or mixtures comprising hydrophobic phytomedicines are: Gingko biloba, Hypericum perforatum, Echinacea purpurea or angustifolia, Ginseng, Piper methisticum (Kava), Tanacetum parthenium, Allium sativum (Garlic),

Examples of lipophilic vitamins include: Carotenoids and lycopene, Tocopherols (Vit E), Riboflavin (Vit B2), Retinol (Vit A), Calciferol (Vit D2), Cholecalciferol (Vit D3), Menadion (Vit K), Folic acid and ubiquinones.

Absorption of lipophilic vitamins is much more limited in comparison to water-soluble vitamins. Fortunately, only very minute quantities of vitamins are required for normal living, however, elderly people who need them more, less effectively assimilate vitamins and essential nutrients. Another population in great need of a sufficient supply of vitamins is the cancer chemotherapy and radiation patients who suffer from mal-absorption syndrome and would benefit from an improved delivery of vitamins and essential nutrients.

A bitter taste compound is any drug, nutrient, vitamin or food supplement or phytomedicine of herbal origin compound, which exerts a rejecting unpleasant bitter bad taste. Bitter taste is associated to hydrophobic compounds or the like, having hydrophobic moiety. Most bitter compounds are lipophilic (fat loving). Examples of bitter taste forming substances that exhibit unpleasant oral taste are: Aloe barbadensis extracts, barbeloins, Artemisia species and various absinthes, gingko biloba extracts, gentian, artichoke leaves, centaury, aloe species, barberry, dandelion, wormwood or mugwort (or other Artemesias) and blessed thistle. Some of the common bitter herbs are dandelion (Taraxacum officinale) and chicory (Cichorium intybus), whose roots have been used in coffee drinks. Beer is made from the bitter hops (Humulus lupulus). Other bitters include: alfalfa, endive, arugula, spinach, unripe apples, citrus peel, scallion, rye, turnip, white pepper, and

celery. The bitterest herb in the medicinal herb garden is wormwood. Some less bitter common nutrients are: hesperidine, limonene, and anthocyanines derived from fruits or vegetables.

Production methods

A) Hydrating and swelling the lecithin in water.

B) Solubilizing the bioactive components in (A) until complete solubilization and visual homogeneity is obtained.

C) Mixing the vegetable proteins with (B) to obtain an appropriate required consistency, adding water if required.

D) Molding, shaping, sieving or granulating.

E) Drying; evaporating the excess water by heat or heat and vacuum combination, by spray dry, or fluidized bed, to obtain a dry homogeneous matrix.

Lecithin is hydrated and swelled in a minimal amount of water (a preferred ratio of lecithin to water is 1:3 to 1:10. The preferred amounts of lecithin, bioactive compounds and hydrophobic ingestibles, are ratios of 2:1 to 1:2 and more favourably, 1:1 on a dry weight basis. The ratio amount of obtained solubilized bioactive compound in lecithin to vegetable protein is 10:1 to 1:2, and more preferably 3:1 to 1:1 on a dry weight basis.

Applied heat and water evaporation converts the vegetable proteins to a state that favours intermolecular interactions.

The composition may be used for oral delivery, taste masking, further enterocoating or coating or immediate release in the mouth. It can also be incorporated in bars, nuggets, solid foods and powders for in situ beverage reconstitutions and the like. The composition may be mixed with flavoring agents such as fruits flavors, natural or artificial, to denote appealing product to the user.

Various delivery systems and dosage forms are possible, including oral capsule tablets or dry suspensions for dilution before use. Instant beverage, instant soup and also incorporation into solid bars or nuggets.

It should be noted that the above descriptions are intended only to serve as examples, and that many other embodiments are possible, within the spirit and the scope of the present invention.

Examples of lipophilic substances that exhibit poor oral bioavailability include: lipophilic drugs, vitamins, NSDA steroids, anti-fungal agents, antibacterial agents, antiviral agents, anticancer agents, anti-hypertensive agents, anti-oxidants, anti-depressants and phyto-chemicals combining herbal extracts.

Low, or poor water soluble compounds, include: fatty sterols of saw palmetto, carotenes and lycopenes, non aqueous soluble fractions of echinacea, ginseng and gingko biloba, in addition to many minerals, such as iron and complex vitamin coenzymes, such as ubiquinones.

After mixing with body fluids, the homogeneous solid matrix composition absorbs water and swells. Following hydration and swelling, the release of the bioactive ingestable takes place in the gastrointestine. The unique matrix and its ingredients as well as the homogeneous dispersion of the bioactive ingestible within the matrix, promotes the solubilization, miclization and emulsification of the insoluble bioactive ingestible, thus enhancing dissolution and bio-availability.

While the invention will now be described in connection with certain preferred embodiments in the following examples so that aspects thereof may be more fully understood and appreciated, it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims. Thus, the following examples which include preferred embodiments will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purposes of illustrative discussion of preferred embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of formulation procedures as well as of the principles and conceptual aspects of the invention.

EXAMPLES

Example 1. Aloe Vera S.D and concentrated soy proteins.

Barbeloin and its derivatives are some of the bitterest extracts. Aloe Vera S.D. (frutarom meer) is a very bitter powder – a non diluted, concentrated extract characterised by a large fraction of many water insoluble ingredients.

A) One gram of soybean lecithin, (Pure lecithin powder, de-oiled, Stern, Hamburg, Germany) was mixed and swelled in 5 ml of water at room temperature.

B) Half a gram of Aloe Vera S.D. dry extract (Frutarom Meer) was added and well mixed to obtain a homogeneous fluid paste.

C) Two grams of functional soy proteins concentrate (Solcon HV, Solbar, Ashdod, Israel), were added and mixed well with QS of water to produce a homogeneous mass in the appropriate consistency for passing through a granulating net.

D) An obtained wet mass was mesh granulated and dried in ovens or microwave ovens.

Three aliquots, equivalent to 10 mg of Aloe Veras S.D. powder in 10 ml of water, were prepared and their bitterness evaluated:

1) Non-treated, Aloe Vera S.D. powder in water was so bitter that it was almost impossible to keep in the mouth, requiring many mouthwashes afterwards, and still leaving a long-lasting bitter taste.

2) Aloe Vera S.D. in water with added lecithin and solcon HV was equally as bitter.

3) Aloe Vera S.D. granules, prepared according to the present example, equivalent to 10 mg Aloe Vera S.D. suspended in 10 ml water was devoid of the original bitter unpleasant taste, and contained no after taste at all.

Example 2. Aloe Vera S.D and isolated soy proteins.

A) 0.5 gram of soybean lecithin, (Phospholipon 90, Natterman, Germany) was mixed and swelled in 4 ml of water at room temperature.

B) 0.5 gram of Aloe Vera S.D. dry extract (Frutarom Meer) was added and well mixed to obtain a homogeneous fluid paste.

C) 1.0 gram of functional soy proteins isolate (Supro EX34K, Protein Technologies International, USA), and 0.5 gram microcrystaline cellulose (Avicel HP101, FMC, USA) were added and mixed well with QS of water to produce a homogeneous mass in the appropriate consistency for passing through a granulating net.

D) An obtained wet mass was mesh granulated and dried in ovens or microwave ovens.

Aloe Vera S.D. soy protein granules, prepared according to the present example, suspended in water was devoid of the original bitter unpleasant taste and after taste.

Example 3, Artemisia abrotantum.

Artemisin and derivatives are also extremely bitter. Artemisia abrotantum (in house hot maceration, commonly called "Shiba") is a very bitter concentrated extract of Artemisia abrotantum, characterised by large fraction of many water insoluble ingredients.

A) One gram of soybean lecithin, de-oiled, powdered (Epikuron 100, Lucas Meyer, Germany) was mixed and swelled in 2 ml of Artemisia abrotantum extract.

B) Two grams of functional soy proteins (Solcon HV, Solbar Ashdod, Israel), was added and well mixed with QS of water to produce a homogeneous mass in an appropriate consistency for passing through a granulating net.

C) Obtained wet mass was granulated and dried in an oven or microwave oven.

Three aliquots equivalent to one ml of Artemisia abrotantum extract in 10 ml of water were prepared and their bitterness evaluated:

1) Artemisia abrotantum extract in water was so bitter that it was almost impossible to hold in the mouth and required many mouthwashes afterwards and left a long-lasting bitter taste.

2) Artemisia abrotantum extract in water with lecithin and solcon HV and slight vortex was equally as bitter.

3) Artemisia abrotantum granules, prepared according to the present example, which were devoid of the original bitter taste, contained no after taste at all.

Example 4. Artemisia abrotantum.

a) 1.0 gram of soybean lecithin, de-oiled, powdered (Pure lecithin powder, de-oiled, Stern, Hamburg, Germany) was mixed and swelled in 10 ml of Artemisia abrotantum extract.

b) 2.0 gram of concentrated soy proteins (Solcon HV, Solbar Ashdod, Israel), and 0.5 gram of soy proteins isolate (Supro EX34K, Protein Technologies International, USA), and 0.5 gram microcrystaline cellulose (Avicel HP101, FMC, USA) were added and well mixed to produce a homogeneous mass in an appropriate consistency for passing through a granulating net.

c) Obtained wet mass was granulated and dried in an oven or microwave oven.

Artemisia abrotantum granules, prepared according to the present example, were devoid of the original bitter taste and after taste.

Resulting granules of Artemisia abrotantum are useful against digestive parasites and are appropriate for use in gastrointestinal disorders that are traditionally treated with Artemisia abrotantum.

Example 5, Gingko biloba and concentrated soy proteins.

Gingko biloba pure concentrated extracts are typical bitters. Gingko biloba (Frutarom Meer, Haifa, Israel) is standardized concentrated 24% gingkolides bitter powder, characterised by the large fraction of many water insoluble ingredients.

a) 0.1 of soybean lecithin was mixed and swelled in 1 ml of water at room temperature.

b) 0.5 a gram of Gingko biloba was added and well mixed to obtain a homogeneous liquid paste.

c) Five grams of functional soy proteins (Solcon HV, Solbar Ashdod, Israel) were added and well mixed with QS of water to produce a homogeneous mass in an appropriate consistency ready for passing through a granulating net.

d) The Obtained wet mass was granulated and dried in an oven or microwave oven.

Three aliquots of equivalent to ten mg of Gingko biloba powder in 10 ml water were prepared and their bitterness evaluated:

1) Gingko biloba powder in water was typically bitter and very unpleasant in the mouth.

2) Gingko biloba in water, mixed with lecithin and solcon HV, was equally as bitter and

3) Gingko biloba granules, prepared according to the present example, was devoid of the original bitter taste and contained no after taste at all for couple of hours.

Example 6, Gingko biloba and isolated soy proteins.

a) 1 gram of soybean lecithin was mixed and swelled in 8 ml of water at room temperature.

b) 1 gram of Gingko biloba, standardized 24% Gingcolides, (Frutarom Meer, Haifa, Israel) was added and well mixed to obtain a homogeneous liquid paste.

c) 2.5 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

d) The Obtained wet mass was granulated and dried in a microwave oven.

Three aliquots of equivalent to ten mg of Gingko biloba powder in 10 ml water were prepared and their bitterness evaluated:

1) Gingko biloba powder in water was typically bitter and very unpleasant in the mouth.

2) Gingko biloba in water, mixed with lecithin and solcon HV, was equally as bitter and

3) Gingko biloba granules, prepared according to the present example, was devoid of the original bitter taste and contained no after taste at all for couple of hours.

Example 7, Gingko biloba instant powder.

The obtained granules of example 6 were ground to homogeneity with instant fruit flavored powders. The resulting powder is reconstituted with tap water to produce in-situ a tasteful beverage. Desired dose of Gingko Biloba extract is delivered in a glass of beverage preferred by those who experience difficulties upon swallowing tablets or capsule.

Example 8, Gingko biloba bars.

Resulting granules of example 6 were mixed with granola and honey or isomaltose premix to produce regular or low calorie and diabetic bar delivering

doses of Gingko biloba extracts without the unwanted bitter taste associated with Gingko biloba extracts.

Example 9, Saw palmetto.

Saw palmetto 90% fatty sterol and lipid (Frutarom Meer, haifa, Israel) is a water insoluble, oily substance that does not mix with water.

a) 0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

b) 0.5 grams of Saw palmetto fatty sterols (90%) was added and well mixed to obtain a homogeneous liquid paste.

c) 1.0 gram of concentrated soy protein (Solcon HV, Solbar, Ashdod, Israel) was added and well mixed with QS of water to produce homogeneous mass in an appropriate consistency ready for passing through a granulating net.

d) The obtained wet mass was granulated and dried in an oven or microwave oven.

Saw palmetto fatty sterols (90%) were mixed in water with lecithin or with functional soybean protein, or both, to yield a non homogogenios dispersion which, after the high energy emulsification step, could be further homogenized to yeald emulsion or related dispersion systems. Saw palmetto, dry powder 25% fatty sterols, (Frutarom Meer) obtained by spray drying Saw palmetto fatty sterols (90%) with filler excipients such as dextrins, were mixed in water and released a separation of the lipids which floated on top of the water within a short period of time.

Obtained granules, whilst dispersed in water, did not release Saw palmetto fatty sterols (90%) and no lipid was floating after many weeks.

Example 10, Ubiquinone, Coenzyme Q10 and concentrated soy proteins.

Ubiquinone is a very hydrophobic water insoluble and lipid soluble solid substance. Ubiquinone was obtained as a solid crystals powder.

a) 0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

b) 0.5 grams of Ubiquinone was added and mixed well, to obtain a homogeneous liquid paste.

c) 1.0 gram of concentrated soy proteins (Solcon HV, Solbar, Ashdod, Israel) was added and mixed well with QS of water to produce a homogeneous mass in consistency ready for passing through a granulating net.

d) An obtained wet mass was granulated and dried in an oven or microwave oven.

Ubiquinone was mixed in water with lecithin, functional soybean protein or both, with very limited yield of non-homogogenios dispersion. A large part of the Ubiquinone was still in crystal particles.

The Ubiquinone was dispersed uniformly in the homogeneous amorphous matrix. The granules dispersed well in water and did not release the Ubiquinone, and no lipid was floating after many weeks.

Example 11, Ubiquinone, Coenzyme Q10 and isolated soy proteins.

a) 0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

b) 0.5 grams of Ubiquinone was added and mixed well, to obtain a homogeneous liquid paste.

c) 1.0 gram of isolated soy proteins (Supro 810, Protein Technologies International, USA) was added and mixed well with QS of water to produce a homogeneous mass in consistency ready for passing through a granulating net.

d) An obtained wet mass was granulated and dried in a microwave oven.

The Ubiquinone was dispersed uniformly in the homogeneous amorphous matrix.

Example 12, Ubiquinone, Coenzyme Q10 and isolated soy proteins.

a) 0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

b) 0.5 grams of Ubiquinone was added and mixed well, to obtain a homogeneous liquid paste.

c) 1.0 gram of isolated soy proteins (Supro 810, Protein Technologies International, USA) and 1.0 gram of microcrystaline cellulose (Avicel PH101, FMC, USA) were added and mixed well with QS of water to produce a homogeneous mass in consistency ready for passing through a granulating net.

d) An obtained wet mass was granulated and dried in a microwave oven.

The Ubiquinone was dispersed uniformly in the homogeneous amorphous matrix.

Example 13, Ubiquinone, Coenzyme Q10 and isolated soy proteins.

a) 0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

b) 0.5 grams of Ubiquinone was added and mixed well, to obtain a homogeneous liquid paste.

c) 1.0 gram of isolated soy proteins (Supro 810, Protein Technologies International, USA) and 0.5 gram of microcrystaline cellulose (Avicel PH101, FMC, USA) and 0.5 gram of fumed silica (Tixosil, Rhone-Poulenc, France) were added and mixed well with QS of water to produce a homogeneous mass in consistency ready for passing through a granulating net.

d) An obtained wet mass was granulated and dried in a microwave oven.

The Ubiquinone was dispersed uniformly in the homogeneous amorphous matrix.

Example 14, Vitamin E.

Vitamin E, Tocopherol acetate is a water-insoluble, oily substance that does not dissolve in water.

a) 0.5 grams of soybean lecithin was mixed and swelled in 5 ml of water at room temperature.

b) 0.5 grams of Vit E was added and mixed well to obtain a homogeneous liquid paste.

c) 1.0 gram of functional soy protein (Supro 810, Protein Technologies International, USA), was added and equally mixed with QS of water to produce a homogeneous mass in a desired consistency ready for passing through a granulating net.

d) An obtained wet mass was granulated and dried in an oven or microwave oven.

Vit E was mixed in water with lecithin, functional soybean protein or both, to yield a non-homogogenios dispersion that after the high energy emulsification step, could be further homogenized to yeald an emulsion or related dispersion system.

Homogeneous dispersion of Vit E was obtained in the granule matrix.

Obtained granules dispersed in water did not release the Vit E and, consequently, no Vit E was floating after many weeks.

Example 15, Lycopene.

Lycopene is a water-insoluble, oily substance that does not mix dissolve in water.

A) 0.5 grams of soybean lecithin was mixed and swelled in 1 ml of water at room temperature.

B) 0.5 grams of 10% Lycopene in tomato oleoresins, (Lycomato, (Lycored, Beer-Sheva, Israel), was added and equally mixed to obtain a homogeneous liquid paste.

C) One gram of functional soy proteins (Solcon HV) solbar hatsor, was added and mixed with QS of water to produce a homogeneous mass in a desired consistency for passing through a granulating net.

D) An obtained wet mass was granulated and dried in an oven or microwave oven.

Vit E was mixed in water with lecithin; functional soybean protein or both to yield non homogogenios dispersion that, after the high energy emulsification step, could be further homogenized to yeald emulsion or related dispersion systems.
Homogeneous dispersion of Vit E was obtained in the granule matrix.
Obtained granules dispersed in water did not release Vit E, and no Vit E was floating after many weeks.

Example 16, Ubiquinone, Coenzyme Q10 and isolated soy proteins.

0.5 grams of soybean lecithin was mixed and swelled in 3 ml of water at room temperature.

0.5 grams of Ubiquinone was added and mixed well, to obtain a homogeneous liquid paste.

4.0 gram of isolated soy proteins (Supro 810, Protein Technologies International, USA) was added and mixed well with QS of water to produce a homogeneous mass in consistency ready for passing through a granulating net.
An obtained wet mass was granulated and dried in a microwave oven.

The Ubiquinone was found to be uniformly dispersed in the homogeneous amorphous matrix.

Example 17, Aloe Vera S.D and isolated soy proteins.

0.5 gram of soybean lecithin, (Phospholipon 90, Natterman, Germany) was mixed and swelled in 4 ml of water at room temperature.

0.5 gram of Aloe Vera S.D. dry extract (Frutarom Meer) was added and well mixed to obtain a homogeneous fluid paste.

5.0 gram of functional soy proteins isolate (Supro EX34K, Protein Technologies International, USA), were added and mixed well with QS of water to produce a homogeneous mass in the appropriate consistency for passing through a granulating net.

An obtained wet mass was mesh granulated and dried in ovens or microwave ovens.

Aloe Vera S.D. soy protein granules, suspended in water was devoid of the original bitter unpleasant taste and after taste.

Example 18, Gingko biloba and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 10 ml of water at room temperature.

1 gram of Gingko biloba, standardized 24% Gingcolides, (Flacksman, Swiss) was added and well mixed to obtain a homogeneous liquid paste.

10 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried in a microwave oven.

Three aliquots of equivalent to a dose of fifty mg of Gingko biloba powder in 100 ml tomato juice were prepared and their bitterness evaluated:

Gingko biloba powder in tomato juice was typically bitter and very unpleasant in the mouth.

Gingko biloba mixed with lecithin and solcon HV, was equally as bitter.

Gingko biloba granules, prepared according to the invention, was devoid of the original bitter taste and contained no after taste at all for several hours.

Example 19, Fish oil and isolated soy proteins.

0.5 gram of soybean lecithin was mixed and swelled in 4 ml of water at room temperature.

2.5 gram of Fish oil, (Denofa, Norway) was added and well mixed to obtain a homogeneous liquid paste.

5.5 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) and 1.5 grams fumed silica (Aerosil 200) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Unpleasant typical fish oil mouth feel taste and smell were masked.

Example 20, Ferrous sulfate and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 8-10 ml of water at room temperature.

1 gram of Ferrous sulfate was added and well mixed.

20 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Three aliquots of equivalent to a dose of 10 mg of Ferrous sulfate in 100 ml tomato juice were prepared and their bitterness evaluated:

Ferrous sulfate was typically bitter and very unpleasant in the mouth. Ferrous sulfate mixed with lecithin and solcon HV, was equally as bitter while Ferrous sulfate granules, prepared according to the invention, was devoid of the original bitter taste and contained no after taste at all for several hours.

Example 21, Ferrous chelate and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 8-10 ml of water at room temperature.

1 gram of Ferrous chelate (ferrous glycinate or ferrous protein hydrolysate) was added and well mixed.

20 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Three aliquots of equivalent to a dose of 10 mg of Ferrous sulfate in 100 ml tomato juice were prepared and their bitterness evaluated:

Ferrous sulfate was typically bitter and very unpleasant in the mouth.

Ferrous sulfate mixed with lecithin and solcon HV, was equally as bitter while Ferrous chelate granules, prepared according to the invention, was devoid of the original bitter taste and contained no after taste at all for several hours.

Example 22, Melatonin and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 10 ml of water at room temperature.

1 gram of Melatonin was added and well mixed to obtain a homogeneous liquid paste.

10 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Melatonine typical unpleasant taste was well masked in the granules.

Example 23, Isoflavones and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 10 ml of water at room temperature.

1 gram of Isoflavones (Solgen 10 or Solgen 40, Solbar plant extracts, Ashdod, Israel) was added and well mixed to obtain a homogeneous liquid paste.

8 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to

produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Three aliquots of samples equivalent to 30 mg of Isoflavones in 100 ml yogurt or tomato juice were prepared and their bitterness evaluated:

Solgen-10 powder was typically bitter aftertaste and unpleasant in the mouth.

Solgen-10 mixed with lecithin and solcon HV, was equally as bitter while Isoflavones granules, prepared according to the invention, was devoid of the original bitter taste and contained no after taste at all for several weeks where kept under refrigeration.

Example 24, Isoflavones and isolated soy proteins.

1 gram of soybean lecithin was mixed and swelled in 10 ml of water at room temperature.

6 gram of Isoflavones (Nutragen-3, Solbar plant extracts, Ashdodo, isarel) was added and well mixed to obtain a homogeneous liquid paste.

3 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried.

Example 25, Isoflavones and isolated soy proteins.

17 gram of soybean lecithin was mixed and swelled in 10 ml of water at room temperature.

6 gram of Isoflavones (Soylife25, Soylife, Netherland) was added and well mixed to obtain a homogeneous liquid paste.

3 grams of functional isolated soy proteins (Supro 810, Protein Technology International, St Louis, MO, USA) were added and well mixed to produce a homogeneous mass or dough, in an appropriate consistency ready for passing through a granulating net.

The Obtained wet mass was granulated and dried in a microwave oven.

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative examples and that the present invention may be embodied in other specific forms without departing from the essential attributes thereof, and it is therefore desired that the present embodiments and examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A homogeneous solid matrix composition, enabling an improved dispersion of and bitter taste masking of hydrophobic, bioactive ingestibles, of at least low water solubility comprising:
   (a) at least 10% w/w vegetable proteins;
   (b) lecithin; and
   (c) at least one ingestible bioactive compound of at least low water solubility.
2. A composition of claim 1, comprising lecithin and said ingestible bioactive compound in relative amounts of 1:3 to 3:1,
3. A composition of claim 1, comprising lecithin and said ingestible bioactive compound in relative amounts of 1:1.
4. A composition of claim 2, wherein the ratio of vegetable protein to the combined amounts of lecithin and ingestible bioactive compound is between 20:1 to 1:2.
5. A composition of claim 2, wherein the ratio of vegetable protein to the combined amounts of lecithin and ingestible bioactive compound is between 4:1 to 1:1.
6. A composition of claim 1, wherein said ingestible bioactive compound has a water solubility of less then 0.5 mg/ml at 25° C.
7. The composition of claim 1, wherein said vegetable proteins are selected from isolated and concentrated soybean proteins, containing at least 50% protein wherein the average MW of said proteins is larger then 25K Dalton.
8. The composition of claim 1, wherein said vegetable proteins are selected from isolated and concentrated soybean proteins, containing at least 60% proteins and said proteins are non-denatured.
9. The composition of claim 1, wherein said vegetable proteins are soybean proteins, containing at least 60% proteins and having a nitrogen solubility index (NSI) of at least 20%.
10. composition of claim 1, wherein said vegetable proteins are soybean proteins, containing at least 70% proteins and wherein the average MW of said proteins is larger then 25K Dalton and the NSI thereof is higher then 20%.

11. The composition of claim 1, wherein said vegetable proteins are selected from the group consisting of concentrated and isolated proteins of: corn, potatoes, wheat, peanuts, beans, rice, sesame, barley, sunflower, canola and rapeseed.
12. The composition of claim 1, wherein ingestible bioactive compound is selected from the group consisting of a drug, a nutrient, a vitamin, a food supplement and mixtures thereof.
13. A composition of claim 1, wherein said ingestible bioactive compound is an herbal extract containing low water soluble ingredients.
14. A method for preparing the composition of claim 1, wherein lecithin is swollen in water in a ratio of between about 1:2 to 1:10 and said ingestible bioactive compound is added until complete solubilization, vegetable protein is then added with additional water to produce granulation dough, whereafter, the wet mass is granulated and dried.
15. A method of claim 14, wherein said wet mass is further diluted with water and spray dried.
16. A method according to claim 14, wherein the wet granulation is extruded through a screen having openings of 0.5 mm to 2.5 mm and spheronized in a spheronizer.
17. A method according to claim 14, wherein said ingestible bioactive compound is a bitter tasting compound and homogeneous particles and taste masking are obtained.
18. A method according to claim 14, in which the wet granulation is prepared and formed into spheres, utilizing a high shear granulator to form taste-masked spheres.
19. The composition of claim 1, wherein the limiting step for the ingestible bioactive compound release is the proteins gasto-intestinal digestion and decomposition of the matrix.
20. The composition of claim 1, wherein ingestible bioactive compound is released over period of one to three hours in the gastro-intestinal tract.
21. A composition of claim 1, which is further coated or encapsulated.

22. A core compound encapsulated with the homogenous matrix of claim 1, in fluidized bad or spray drying process.